Complementary and Alternative Medicine (CAM): A Review for the Primary Care Physician

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It is difficult to find a satisfactory title for this review, because both the word "complementary" and "alternative" are not very politically correct currently. It is probable that there is no fully politically correct word, except for "non-allopathic," which is unfamiliar to many MDs. Accurately used, the term "allopathic" is as opposed to "homeopathic," so from its origins, "allopathic medicine" should include herbal medicine. However, in practice, herbal and many other non-homeopathic treatments are called "non-allopathic," whereas conventional medicine is called "allopathic." "Complementary" usually would include practices that are used ***with*** *conventional western medical treatments, and "alternative" would include those practices that are used* ***instead*** *of western medical treatments. For most of this review, the terms "non-allopathic," "alternative," and "complementary" could be used interchangeably.*

This topic has gained interest, and received some allopathic legitimacy, in part because of an article that David Eisenberg, M.D., published in the New England Journal.[1] In 1990, he performed a telephone survey of about 1,500 adults in the U.S. and asked them about the use of treatments and practices that were "alternative," which he defined as not generally being taught in the U.S. medical schools and not being readily available in U.S. hospitals. From his sample, he extrapolated that in 1990, about 60 million Americans used alternative medical treatments, at an estimated cost of $13.7 billion. There were more visits to alternative healers than to primary care MDs that year, and over two-thirds of people who did use alternative medical treatments did not tell their doctors about it.

Now that third party figures are becoming interested in paying for alternative medical practices (especially naturopathic, chiropractic, and acupuncture services), allopathic physicians will be increasing in the position of being able to refer people to alternative providers, and insurers will pay for services that MDs approve. Therefore, it will become increasingly important for physicians to have a degree of familiarity with alternative treatments (including efficacy and risks). So far, to date, there have been no cases of malpractice for giving advice about the use of alternative medical treatments, but liability will certainly exist to anyone who delivers treatments, such as acupuncture or spinal manipulation, in the event of an adverse effect.

This review will briefly introduce some of the most common alternative practices likely to be seen in Hawaii communities: Homeopathy, Herbs, Naturopathy, Chinese Medicine and Acupuncture, and Chiropractic and spinal manipulation, and a brief discussion of Dr. Eisenberg's recent position paper on advising patients about alternative practices.

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Homeopathy

Homeopathy was invented by Samuel Hahnemann, a physician who lived from the mid-1700s to the late 1800s. He was alarmed by the rather toxic nature of medical treatment of his day: it was common to treat by purging or bleeding, and it seemed to him that the doctors were often doing harm in their treatments. (This is a recurring theme among the founders of alternative methods.) He wanted to find some treatment method which was gentle, and which would cause no harm.

In the early 1800s, he revisited an old idea which Hippocrates had promoted, that of the "Law of Similars": *simila similibus curentur* (like cures like). The idea occurred to him after he took an overdose of quinine (cinchona bark) and became ill with it. He noticed that when he got sick, his symptoms were similar to those of malaria. At the time, physicians knew that quinine cured malaria, though they did not know the cause for malaria. Hahnemann surmised that perhaps it is because quinine **mimics** malaria that it is capable of **curing** malaria, if taken in lower doses. It is taking a "simillimum," a substance that can mimic the illness, which will cure the illness. Hahnemann thought that the similar drug would activate some vital force in the body to react against the illness.

He advanced his idea to his colleagues, and together they set about the task of "**proving**" drugs: identifying what symptoms they caused in high doses, in order to match them up with illnesses, after which they would be diluted down to non-toxic doses. Hahnemann chose "reliable observers" (including himself), who would take a large dose of a medicine, usually herbs and minerals that were used medicinally at the time, and note down what the symptomatic results were. They pooled several observers' findings and identified what each drug's signature symptoms were. This process is called "proving" a remedy.

They tried to identify the minimum dose of each drug that would be effective as a cure. To Hahnemann's surprise, he discovered that no matter how far he diluted the drugs, they still seemed to work as cures for illnesses. The explanation for this was that the method of

dilution could be releasing some aspect of the original substance into the diluent (usually distilled water or alcohol solution). Hahnemann developed the dilutional method called **succussion**, wherein very precise dilution of the drug would be measured, and the container with the dilution would be pounded gently with a felt pad in a precise way, and then that solution would again be precisely diluted again, and pounded again. This method would activate the water or alcohol solution, which was being used as the diluent. If there was a substance that was not soluble in liquid, it could be ground up with milk sugar, (which was considered an inert substance) and that is called **trituration**. For every substance, the observers noted that the more dilute it became, the more potent it became. So in homeopathy, dilution is the equivalent of **potency**, and the act of dilution is called potentization, or **potentiation**. This is the opposite of what conventional medical doctors usually think of as "potency." In homeopathy, higher potencies are considered to be more powerful and able to stir up the body's "vital force." In classical homeopathy, patients can only get the extremely dilute (potent) medicines from a licensed practitioner and can't buy them over-the-counter.

Labeled homeopathic medicines denote potency by two methods. In Europe, they use the "decimal system" which is denoted by the symbol "x." 1x is diluted 1:10, and 2x is 1:100 (1x diluted with 9 parts diluent), etc. The "centesimal system" is denoted by the symbol "c" and is used more America. It starts with 1c= 1:100, and each successive dilution is 1 part to 99 parts diluent, so 2c is 1:10000, adding two zeros with each additional dilution.

Hahnemann and his colleagues thought through the mathematics, and realized that there is a point where the dilution is likely to become pure water, with a very high likelihood that there are no molecules of the original drug left in the solution. When this point is reached it is called **ultramolecular dosing**. This happens at 12c or 24x, where one can be almost 100% sure that there will be nothing of the original substance left in the homeopathic remedy. This became a source of controversy, and some people who practiced homeopathy thought that efficacy at ultramolecular doses defied logic, and chose to use only the lower potencies. Today, most homeopathic practitioners agree that high potencies do work better than low potencies, even at ultramolecular doses.

In classical homeopathy, it is considered ideal to use only one individualized, single simillimum in the treatment of an illness. Much of the "art of homeopathy" is that of choosing the correct simillimum. This is accomplished by means of a very careful history and exam, as well as incorporating knowledge of the type of person the patient is (body type and personality type). The practitioner then picks the one salient symptom of their illness to match with a simillimum. In classical homeopathy, a single individualized remedy is chosen, but in modern homeopathy treatments are often combined, especially in lower-potency OTC proprietary homeopathic remedies. There is some ongoing controversy within the homeopathic community about whether multiple remedies are effective or not.

Individualization is a hallmark of classical homeopathy, and this has been a problem when it has come to developing randomized trials. Many homeopathic practitioners will not accept trials without individualization as valid tests of the efficacy of what they do, since all their practice involves individualized remedies. The same criticism applies to the use of multiple remedies, which have commonly been used in clinical trials. Hahnemann described one situation when individualization was not used and that was for epidemics. During a scarlet fever epidemic, he used belladonna as a *remedy epidemicus*, and gave it to all patients for both treatment and prophylaxis, reportedly very successfully.

In practice, homeopaths use two main types of references: a *materia medica*, or book that lists the symptoms that drugs can cause, and a *repertory*, or index of symptoms and what remedies might match. The selection of the potency to use is part of the "art" of homeopathy, but there are several principles involved. Treatments for mental symptoms are usually prepared using higher potencies than those for organic symptoms. Treatments for older patients are usually made with lower potencies, since older patients can't tolerate the stirring up of the vital forces produced by high potencies. Children usually are treated with higher potencies.

If patients are not improving with homeopathic remedies, practitioners will often review the remedy they chose. In particular, the higher potencies must be well selected and are only supposed to be effective if the right simillimum is used. So, if a practitioner finds his/her patient is not finding symptom relief, they will review the history again and perhaps start a new remedy. Also, in homeopathy, treatment will classically produce a "homeopathic aggravation" before the illness starts to improve. Practitioners have often supported patients through the aggravation period with placebo use and this is an accepted practice. Of interest, one aspect of homeopathy is that practitioners tend to campaign against fluoridation of municipal water supplies, with the belief that small doses of fluoride added to the city water can become naturally succussed as the water travels through the city's pipes. This would, in turn, lead to mass exposure to a potentially toxic potency of homeopathic fluoride. So, homeopathy enthusiasts may be active in anti-fluoride citizen's action groups in metropolitan areas.

In order to clarify what homeopathic remedies are, the following are examples of a few common remedies dispensed to patients:

(1) Allium (onion): this is used for neuralgia pain, illnesses with weepy eyes.
(2) Apis (ground up honeybees): this is used for stinging pain, blisters, and fever with dry skin.
(3) Arnica (toxic flowering herb): used for shock, pain, bruising, and injuries (arnica is used topically in herbal medi cine for injuries).
(4) Ipecac (herb): this is used to prevent/treat vomiting.
(5) Belladonna (herb): for illnesses that mimic anticholinergic symptoms, like flushing, hot fever, and dilated pupils.

Now that we have reviewed the underlying beliefs and practice of homeopathy, the question for conventional practitioners is clear: does homeopathy work? There is a body of clinical investigation on homeopathic remedies.

An excellent overview of homeopathic research is found in an article by three researchers from the Netherlands[2] and published in the *British Medical Journal* (BMJ) in 1991. Their conclusions led to a huge controversy, and the BMJ received more mail in response to this overview than they ever received from any prior article. It is a meta-analysis and overview of clinical trials of homeopathic treatment. The investigators reviewed 107 trials, but 2 of these were comparing one homeopathic treatment with other homeopathic treatments, leaving 105 trials that compared homeopathy with

placebo or standard medical treatment. Of these, 81 indicated positive results (homeopathy is likely to be effective), and 24 found no evidence of effect. Most trials had relatively poor quality methods but there were some that were that were well designed. The authors considered it likely that some publication bias existed. Publication bias can work in favor of, or against publication, depending upon the orientation of the editors. Alternative medical journals would theoretically be more likely to want to publish items that had positive results for alternative treatments, but conventional medical journals would be more likely to want to publish negative results. However, review of the outcomes does not reveal any correlation between the orientation of the journal (alternative vs. conventional) where an article was published and whether it demonstrated positive or negative results.

Of the best quality trials in homeopathy, 15 had positive results, and 7 did not. The authors of the BMJ overview indicated that there is some evidence that homeopathic treatment can be efficacious in the following illnesses: respiratory infections, hay fever, asthma, GI complaints (especially gastritis and irritable colon), arthritis pain, migraines, and recovery from sprains. Most trials were with polypharmacy (multiple combined remedies), and/or did not have individualized treatment, which has been a source of criticism by the many homeopathic practitioners.

Herbal remedies

This will be a brief review of some of the current oversight (or lack of it) on herbal medicines, some of the most commonly used herbs, and a review of a few herbs with documented toxicities.

The U.S. law currently does not provide good oversight of herbal remedies and dietary supplements and there is some work being done to improve the regulation of these products. Other countries have done a little bit better than the U.S. in crafting legislation. Currently, the U.S. is following the Dietary Supplement Health and Education Act of 1994. Senator Oren Hatch of the state of Utah (which has an active herbal products industry) introduced this law. It permits the marketing of "dietary supplement" with no required approval of any government agency, so long as there is a label on the product that states that (1) no Food and Drug Administration (FDA) evaluation of that product has occurred, and (2) the product "is not intended to diagnose, treat, or prevent any disease." When these criteria are met, the burden of proof about the product's safety, or lack of it, would rest entirely on the FDA, and not on the manufacturer of the herbal/dietary product. In practice, no one is actually taking responsibility for the safety of products, unless the FDA chooses to try to prove that a product is unsafe. The manufacturers can suggest doses on the label and these products are not standardized.

Other countries have better rules. For example, Germany gathered together a group of experts, called the German "Commission E," which was in effect from 1978 until 1994. This commission included toxicologists, pharmacologists, physicians, and other scientists and they produced 400 monographs on herbal medicines. They reviewed the available evidence, using a standard of "reasonable certainty of efficacy" and then produced guidelines for their use, dosing, and administration. The Commission E's monographs are available in English in the U.S., though more scientific evidence has been accumulating since they were published.

In contrast, in the U.S., in order to obtain FDA approval for a drug, a company would need to provide evidence and meet a standard of "absolute certainty of efficacy," and the average cost to achieve that standard is now about $350 million per drug. Since none of these

herbs or dietary supplements is capable of having a patent on them (a patent would make the investment worthwhile in future profits), no company would be willing to try to meet that FDA standard. So, unless the U.S. derives a separate category for herbs/dietary supplements or any non-patentable health products, to allow for a less-rigorous (and economically feasible) standard of efficacy, these things will never receive the funding for the research necessary to become FDA-approved. Hence, they will lack standardization, federal controls, or even testing to see if they are safe or effective. Many sources of information about herbs recommend that prior to using an herb, the patient should discuss its use with their physician, making it important for physicians to know about common herbs used and their safety and efficacy.

In general, Western herbalists will use medicinal herbs either singly, or mixed in combinations. In Asian cultures, it is very unusual to see a single herb prescribed; usually prescriptions are for herbal mixtures. There tends to be a common belief among herbalists that the "naturalness" of the product makes it balanced, and safe. Many patients will not take any purified extracts of herbs, with the belief that if a substance is purified, then it will take away its natural balance and it may destroy its positive attributes. The scientific studies on herbs are in general small in number, and most of them are not well done. Many of them are tested only on animals, or using very small numbers of patients, or are not randomized or controlled or blinded adequately, or are only *in vitro*, and many of them aren't available in English.

The following is a very brief review of some of the commonest herbal remedies and dietary supplements being used by patients today:

St. John's Wort, or Hypericum. This is a widely used herbal remedy for mild to moderate depression, and possibly for anxiety (there is a trial ongoing regarding its efficacy for anxiety). There are some well-designed small clinical studies on St. John's Wort, unlike many of the other herbal products used. A large long-term National Institute of Health (NIH) trial is ongoing. In the studies to date, it has demonstrated efficacy equivalent to imipramine in some.[3,4] It's been safe in the studies to date, much safer than the tricyclic antidepressants, and with far fewer side effects. In the German commission E report monograph on St. John's Wort, it is described as having an monoamine oxidase (MAO) inhibitor-like mechanism of action, based on two older studies. Subsequently there has been more research produced about it and it has been shown to have only trace MAO inhibitor effects at clinically relevant doses. There is some recent evidence that it acts as a combined seratonin, epinephrine, and dopamine reuptake inhibitor.[5] Because of the seratonin effects, it may be wise not to combine it with MAO inhibitor use. Hypericum is very popular, and is receiving considerable coverage in the lay press, but long-term studies are needed. It is the most commonly used anti-depressant in Germany, where it is prescribed three times more than any of the antidepressants used in the U.S.A. The *British Medical Journal* published an overview and meta-analysis in 1996 entitled, "An Overview and Meta-Analysis of St. John's Wort for Depression".[3,5] They reviewed and combined data from 13 trials comparing Hypericum with placebo, and demonstrated a positive effect on depression, with 55% response to the herb compared to 22% responding to placebo. Then they compared it with tricyclics, specifically imipramine, 64% responded to Hypericum with 58% responding to the imipramine. So, it appears to be at least as efficacious (and possibly more efficacious) than the tricyclic antidepressants. It has not been compared to the SSRI antidepressants in clinical trials. Side effects were very similar to placebo, and significantly less than those taking trycyclics. The main side effect documented for Hypericum is photosensitivity, which can occur with large doses, though this appears unlikely at usual doses. The time frame for these studies was short, with only eight weeks maximum follow-up.

Echinaceae. Echinaceae was reported to be the most commonly purchased herb in the U.S. in 1996-7. There are three different species of Echinaceae sold: *E. angustifolia, E. purpurea,* and *E. pallida.* It's available as a root extract or tincture, and very popular for use to treat viral URI's. It is used as an "immune booster" and to treat colds and other viral and bacterial infections. There are several published studies on Echinaceae, but with a paucity of large randomized controlled blinded clinical trials. Animal and *in vitro* studies demonstrate increased cell-mediated immunity, enhanced macrophage activity, increased phagocytosis, and one Echinaceae species seems to have antistaphylococcal and antistrep activity. The herbal literature advises it for short-term use only, because it may activate the immune system. So, most lay sources advise against its long-term use, for fear of inducing autoimmune illness, and against its use at all in patients who have any autoimmune illnesses such as SLE, rheumatoid arthritis, or multiple sclerosis. However, there are no controlled studies to indicate that autoimmune flares have been a problem with the use of Echinaceae. Toxicity is reported to be rare and most evidence to date suggests that Echinaceae seems safe.

Uva Ursi or bearberry, This is an evergreen shrub, found in the forest of North America. It is an old Native American herb, used to treat and prevent urinary infections. The leaves are chewed and eaten, and are available as pills. This herb appears likely to be safe, with no reported toxicities, but the paucity of good data on safety and efficacy make it difficult to recommend.

Saw Palmetto *(Seranoa repens).* Commercial extract of saw palmetto (including one called Permixicon) is increasingly used by men who take it to relieve benign prostatic hypotrophy (BPH) symptoms. The farmers in the southern U.S. are happy about this: the plant is a weedy little palm which takes over the fallow fields, and farmers must pull the plants out before they can replant their crops, but now they can sell their erstwhile weeds on the market. There is some data to indicate that it may help relieve symptoms of prostatism, and toxicity in trials to date has been negligible. It contains a mixture of chemical compounds and has activity on several levels: there is slight 5-alpha-reductase activity, but likely too little to be clinically significant, and in trials there has been no effect on PSA levels, which should drop if there is significant 5-alpha-reductase action.[6] It has been shown to block binding of dihydrotestosterone to prostate cells' androgen receptors, and this is the most popular current theory for its mechanism of action. One European trial showed the extract to have similar efficacy to finasteride, and small trials comparing it to alpha-blockers have shown no significant differences in efficacy.[7] All trials are hampered by the presence of large placebo effects consistently found in trials about treatment for

the symptoms of BPH. Larger placebo-controlled trials are sorely needed.

Garlic ***(Allium sativum)*** seems to lower cholesterol, and inhibits clotting. It has evidence of fibrinolytic activity and it lowers platelet aggregation *in vitro*. It may help lower blood pressure; there have been studies with divergent results on garlic's effect on treating high blood pressure. There is indirect evidence that it may have an antibiotic effect, and it has been touted as helping to treat colds and yeast infections. It has ingredients that are antibacterial but whether it works as such when ingested is not that clear. Some herbalists say it ought to be eaten raw instead of cooked, because cooking seems to inactivate its main pharmacological ingredient, allicin. The best effect was seen with very high doses, which will be equivalent to 5-20 raw cloves a day for a 175 lb. person; this might be socially problematic! There were 2 meta-analysis by different researchers out of Oxford, England in 1993.[8,9] Each reviewed studies with standardized powdered garlic (with a standardized allicin content). They had conflicting results, and they came up with opposite conclusions. More recent trials have also had conflicting results, some showing significant decreases in serum LDL cholesterol, and others showing no effect. The discrepancies may depend on the garlic preparation used. The upshot is that garlic **might** lower cholesterol, and it **might** lower blood pressure. It is unlikely to have adverse effects beyond halitosis, though some experts recommend that patients not take garlic supplements if they are anticoagulated, for fear of additive effects.

Feverfew is used for migraine headaches. Two or three fresh leaves are supposed to be ingested every day, however, it is usually not sold as fresh leaves. It may have a spasmolytic effect, similar to methysergide or parthenolide. It has indirect anti-seratonin properties on animal tissue *in vitro*.[10] Its clinical efficacy has not been demonstrated with well-designed large clinical trials. Many commercial preparations available in the U.S. seem to have a minute amount of the herb, which is unlikely to have any effect. It appears safe thus far but good studies are needed.

Valerian is probably the most commonly prescribed sleep medicine in Europe. It is from the root of the plant *Valeriana officinalis*. It has been used medicinally to induce sleep for thousands of years. It has an ingredient that binds to the benzodiazepine and other receptors in the brain, and it has sedative properties. It is available as a tincture, or freeze-dried extract capsules. Its safety seems well established, especially considering its widespread and long-term use. A published case report of an intentional overdose showed that its toxic effects were very mild. In some small studies, it doesn't seem to cause any addiction or rebound insomnia when it is discontinued, but larger well-designed studies are needed.

Dong Quai or Tang kuei. *Angelica sinensis* is the Latin name for this medicinal plant, which has been called "the female ginseng," and it is often used for various gynecological ailments. It is purported to have weak estrogen-like activity and so some literature has advised avoiding use of the herb for patients who have breast cancer. However, it does not have phytoestrogens, and research to date has not been able to clearly identify whether it does have any estrogen activity. It does contain several courmarins, which are vasodilators and antispasmodic, though the utility of these effects has not been well-defined. Clinically, it is being used for menopause, menstrual irregularity, PMS symptoms, and as a women's general "tonic" (a word used frequently to describe herbal medicines, meaning that it helps people adapt to their environment, keeping them healthy, and making them feel more energetic). It appears to be safe in the usual doses but studies are lacking. It is popular right now, especially for treating menopause symptoms.

Ginseng ***(Panax ginseng).*** There many different plants that are sold under the name "ginseng," but the genus *Panax ginseng* is the source for true ginseng root. Adulteration and the use of other plants called Ginseng (e.g. Siberian Ginseng, American ginseng, etc.) are a problem in identifying its characteristics. True ginseng root is very expensive; it takes six years to grow a crop and it is easily and commonly adulterated, and easily inactivated by processing. Ginseng is supposed to be an adaptogen, or "tonic" and is thought to be antifatigue and antistress. It was thought to have some estrogenic activity, but recent studies have not found any evidence of direct estrogenic effect. It might induce hypertension in some individuals. Ginseng is a classic example of the "doctrine of similars," which is found in all cultures. The "doctrine of similars," states that there is some physical clue about the plant which tells you what malady it will be useful for. For example, if a plant has yellow sap, it would be useful to take it for jaundice. Ginseng root grows in various shapes, but it often looks like a little person: it may look like it has arms and legs, and herbalists have taken this as a sign that it is supposed to be for the well-being of the whole body. It also often looks phallic, and at times even a bit like female genital labia, so it has been purported to be useful for male potency, and as an aphrodisiac for males and females. Ginseng has apparently been studied to see if has any aphrodisiac effect, with good evidence that it does not have any effect as an aphrodisiac. However, it is still marketed as such, and herbalist literature states that it is useful to improve the sex life. (There are a countless other interesting examples of the "doctrine of similars." For example, there is a leaf that the South Americans use which is quite stiff and if it is crumpled up, it will pop back into shape, and that leaf is also used as a male aphrodisiac.)

There are many varieties of ginseng, and it is often not labeled correctly. There is adulteration and often processing inactivates it. All of this variability has made it hard to investigate reported toxicities. There have been reports published of ginseng toxicities, and the product when investigated has been found to not have any ginseng. There are no good studies that demonstrate ginseng's effectiveness. It is probably safe, based on the thousands of years it has been used, but adulteration makes it very hard to be certain.

Ginkgo biloba. Ginkgo leaves come from an ancient tree species; it has been around since the ages of the dinosaurs. It is hardy and grows in cities all over the world. A standard extract is produced from the leaves which contains 24% flavinoids and 6% terpenes; tablets always have 40 mg of the extract. It is easy to standardize and relatively inexpensive and commonly available, so it is easier to study this herb than one like ginseng. Its use is primarily to prevent or improve memory loss, especially in the elderly, and a recent article in JAMA demonstrated a small but significant effect on

decreasing progressive memory loss in patients with mild dementia.[11] It is supposed to improve cerebral blood flow, and some studies have indicated a possible positive effect for other neurological ailments including headaches, tinnitus (especially if it has a CNS source) and depression. There is one study published in the *Aviation, Space, and Environmental Medicine Journal* in 1996.[12] The authors did a randomized controlled trial of an extract of ginkgo biloba 761 used for altitude sickness during a Himalayan expedition. There were 44 men in the study. They randomized them and gave half of them 80 mg orally BID of standardized ginkgo extract and compared them to a double-blinded placebo group. The results were striking: none of the ginkgo group developed signs of cerebral mountain sickness vs. 40.9% developing such symptoms in the placebo group ($p= 1.4 \times 10\text{-}3$). The difference was also striking for respiratory symptoms and high altitude pulmonary edema (HAPE): three in the ginkgo group developed respiratory mountain sickness symptoms (13.6%) vs. eighteen (81.8%) in the placebo group ($p=1.2 \times 10\text{-}5$). Since prior studies had indicated that ginkgo had a positive effect on improving circulation to the extremities during cold exposure, the researchers took a plethysmography device along on the climb up the mountain. Then they checked the study participants for both objective evidence of compromised blood flow of their extremities with plethysmography, and a questionnaire about symptoms of vasomotor constriction (stiffness, numbness, aching). These were also highly significant and demonstrated a marked improvement of peripheral circulation among the study participants who took ginkgo. This study has attracted virtually no notice in the medical community, and perhaps it needs to be repeated to see if it can be replicated in a larger population before ginkgo can gain acceptance as a possible safe and efficacious preventative for acute mountain sickness and frostbite. It increases arterial and capillary vasodilatation, and it slightly lowers clotting time, so it should be used with caution in people on aspirin and blood thinners. A reported overdose of Ginkgo caused restlessness, nausea, vomiting and diarrhea. This is an herb which is ripe for well-controlled sizable trials.

Glucosamine is a constituent of cartilage glycosaminoglycans. This is sold as a dietary supplement. Glucosamine stimulates cartilage cells to produce glycosaminoglycans and proteoglycans, which may allow restoration of cartilage in intra-articular destructive diseases. There have been trials, all short term, that have shown that it's effective in relieving pain and increasing range in motion in osteoarthritis. A four week double-blind trial in 252 osteoarthritis patients demonstrated that glucosamine was significantly superior to placebo.[13] In another four-week trial on 200 patients, it was as effective as ibuprofen 400 mg tid from the second week on.[14] Glucosamine seemed slightly slower to relieve symptoms, but subsequently it works as well (or better than) ibuprofen. A double-blind eight-week trial with 40 osteoarthritis patients randomized to two groups: one group took 500 mg glucosamine tid and another took ibuprofen 400 tid.[15] This study demonstrated that ibuprofen and glucosamine were as about equally effective during the first two weeks of the trial, and by week eight, the glucosamine group was doing better. Another study demonstrated that the positive effect of glucosamine on arthritis symptoms seems to last for a week or two after stopping the drug, unlike NSAIDs. In all trials, glucosamine is well tolerated. Any side effects were equally as common in the placebo group. Commercially, it is often combined with chondroitin sulfate. There are no good studies that I have found on the efficacy of chondroitin but there was a popular book called The Arthritis Cure, that was a bestseller last year. The author claimed that glucosamine should be combined with condroitin for maximal efficacy, and now they sell preparations with the two combined in the ratio he proscribed. There was a recent review in *The Medical Letter* (a conservative and respected publication), in September of this year.[16] Their view was that glucosamine is safe and possibly effective, but there is a need for longer trials. As they have with all "dietary supplements" that they review, they caution with the fact that this is a dietary supplement, so you never know if what you are buying is what is on the label. The NIH's Office of Alternative Medicine is currently funding a large trial on both glucosamine and chondroitin in the treatment of osteoarthritis.

Toxicities from Herbs

There are some important herbal toxicities that practicing physicians should be aware of.

Germander. This is an old time drug used to treat diarrhea and used topically for oral lesions. It was found to cause hepatitis and its use has been banned in France, but is still readily available in the U.S.A. It's especially worrisome when patients combine it with other potential hepatotoxins.

Chaparral. This is an old American Indian remedy. This is used for **everything** (always a good warning sign that an herb is probably not good for anything!), including arthritis, cancer, VD, tuberculosis, URI symptoms, as a hair tonic, and to remove LSD from your system. It has been conclusively proven not to remove LSD from your system, by the way. There is an ingredient in chaparral that has very potent antioxidant qualities called NDGA, which has no proven medical value, but it has been shown to increase the life span of a mosquito from 29 to over 45 days. Nevertheless, chaparral was removed from the Generally Recognized As Safe (GRAS) List in 1990 because it causes subacute hepatic necrosis.[17,18] You can still buy it in health food stores in the U.S.

Comfrey is an old-time remedy and its name sounds like it should make the ill well again. It comes from the plant *Symphytum officinale*, and it is used for many different illnesses, something of an herbal "wonder drug." It used to be called "knit-bone," and was applied externally as a poultice for broken bones and internal injuries. The tea has been used to treat peptic ulcers, it is purported to "purify the blood," in addition to being recommended for almost any ailment you can think of. All comfrey products tested have contained hepatotoxins called pyrrolizidine alkyloids. There are several herbal remedies in various countries with these same toxic ingredients, including "bush tea," and "gordolobo tea" in Central America and Mexico; these also contain pyrrolizidine alkaloids.[19] They can cause liver cell necrosis and veno-occlusive disease in lungs and liver. Veno-occlusive disease can cause pulmonary hypertension, and there have been several documented cases of comfrey-induced pulmonary hypertension. The toxicities seem to be related to the total dose, host susceptibility and route of exposure, with the root being considerably more likely to have significant levels of toxic

alkyloids than the leaves. It's been banned in Great Britain and in Canada, but you can still buy it here in the U.S. Upon review of several of the herbal books at a local bookstore, several had sections extolling the virtues of Comfrey, with nothing about potential health problems or any indication that the herb has been banned in other countries.

Scullcap ***(Scutellaria lateriflora)*** is commonly used for "female weakness," as a tonic, and it is purported to have tranquilizing and antispasmodic activities. The studies done on it to date have failed to find any effect at all, so it seems doubtful that it has any medicinal value. It was reported to be hepatotoxic in four women who were using it to treat stress. Subsequently, the investigators had reason to wonder if this was actually caused by a Germander substitution. It is not really clear that the scullcap is toxic but there have been published warnings about possible toxicity.[20]

Sassafras ***(Sassafras albidum)*** is what old-time root beer used as a flavoring and it was used as "spring tonic". It has safroles and allylbenzenes which have been proven to cause cancer in mice. It is not clear if it is carcinogenic in humans because we don't have the enzymes that change the sassafras ingredients into the carcinogenic substances, so we probably don't have the risk of carcinogenesis that mice have. It is not clear if it should be banned, but right now it is prohibited by the FDA as a flavoring or a food additive based on the murine studies. However, you can still get it as an herbal remedy, primarily in sassafras tea. There is no evidence that it does anything medically at all, so it may be prudent to advise avoidance of this herb as long as there exists doubts about it's safety.

Naturopathy

In order to be licensed as a naturopath in Hawaii, a practitioner must have a N.D. degree, obtained from a four-year naturopathy school. There are two such institutions in the Pacific Northwest, one in Arizona, and there are others opening in the East Coast. Their training is like medical school, their first two years are basic science, pathology and other basic sciences, and the latter two years are devoted to study about herbal medicine, homeopathy, nutrition and lifestyle changes, which are the basics of modern naturopathy. Most schools teach something about spinal manipulation, and spend considerable time teaching counseling techniques, and some teach some acupuncture, although usually that would be taught at a separate institution. The training in the last two years is in the outpatient clinics that are affiliated with the schools.

Naturopathy started in Germany, again as a result of physicians' horror at the toxicity of the commonly used medical treatments. Early naturopaths were interested in "water cures" where they gave patients pure spring water to make them better, and they used treatment intended to build up the healing power of nature, with emphasis on gentle, nontoxic remedies. A naturopath interviewed here on Oahu indicated that about two-thirds of his practice was pain treatment, adjunctive cancer care, chronic allergies, chronic arthritis, chronic GI problems (especially irritable bowel, chronic nausea) and menopause and PMS. Some naturopaths interested in women's

health may have most of their practice treating menopause and PMS. Basically, naturopaths often treat illnesses that conventional physicians don't have reliably safe or effective treatments for. Naturopaths can order diagnostic tests and they can give homeopathic treatments but they don't have a license to prescribe drugs.

Chinese Medicine

Like many complementary medical systems, Chinese medicine is based on the idea that illness arises out of a life or body force that has been disrupted or placed out of balance. Chinese medicine is based on the idea of Ch'i, the life force. In Chinese medicine, all of life is Yin or Yang, and sickness is due to the imbalance of these two opposites. All medical care is directed to adjusting the balance. The concepts of Yin and Yang are complex. Yin is cold and female and Yang is hot and male, but it is much more complicated than that.

The Chinese system of medical diagnosis is very different from anything that is taught in western medical schools. There is extensive emphasis on using the pulse for diagnosis. There are six different pulse points with three depth levels for each pulse point. Chinese practitioners take the pulse very carefully and they make the diagnosis from the character of the pulses. In addition, the tongue is also used for diagnosis, and Chinese texts may have many pictures of tongues that tell you what the diagnosis is. In addition to the pulse and tongue diagnoses, practitioners depend on general observation of the patient. The diagnoses are not like anything that western physicians are familiar with. The nomenclature is entirely different, with symptom complexes that are grouped together in ways entirely different from any western symptom complexes. Since the language for illnesses is foreign from Western medicine, it is very difficult to translate back and forth. "Stagnant blood" is one of the most common diagnoses, and "extravasation" is frequently referred to as a common illness. It is very confusing to try to make sense of Chinese medical books after learning about illness from a European perspective.

Chinese herbs are given in formulae or combination, and it would be unusual to have a single herb given. Herbal formulae are usually steeped as a tea, often unpleasant-tasting. There are over 7,000 different herbs that are used in Chinese medicine. Patients will be prescribed a bag with a mixture of herbs, and it is not uncommon for the herbalist to use substitutions by accident or on purpose, which makes it very difficult to track ingredients or the source of any toxicity. In general, toxicity from Chinese herbs is quite uncommon. Of the150 commonest herbs given, about 10 of these have clearly had instances of reported toxicities. But most of the herbal formulae have been used for many thousands of years. Cases of severe or fatal poisoning do occur with both Chinese herbal medicines and Chinese proprietary medicines (packaged pills with combinations of drugs for a specific ailment, e.g. "Dr. _____'s arthritis formula"). Both herbal and proprietary medicines have been contaminated with serious toxins and prescription drugs, including heavy metals, steroids, potent NSAIDS and substituted cheaper herbs. The main toxic effects from Chinese medicines are from a few things that are used: podophyllin, aconites and anticholinergic effects from things that are often used in asthma medicines.

There is an example of a Chinese proprietary medicine, Chuifong Toukuwan, called by most of the westerners who used it "black balls from China." The pills look like little gumballs and they were used for arthritis. There is a published report of thirteen American patients taking this for rheumatoid arthritis and they all improved markedly when they were taking it.[21,22] However, then they developed side effects, including ecchymoses, Cushingoid appearance, diabetes, hypertension, arrhythmia, weight gain, and one had compression fracture and one had bone marrow suppression. When the medicine was analyzed, it was found to contain indomethacin, prednisone, small amounts of lead, and aminopyrine (a very toxic substance known to cause bone marrow failure). Also, when the patients stopped taking the first batch and started the next batch, all had a flair of their arthritis symptoms, indicating that they probably received quite different ingredients in the second batch. So it would be wise to caution patients not to take unlabeled, proprietary medicines.

Acupuncture

Acupuncture is based on twelve meridians, or lines of energy, in the body. Acupuncture points lie on the meridians. Meridians don't necessarily follow the nerve pathways. It is clear that acupuncture releases endorphins, and it changes the electrical conductivity of the skin. Whether that has anything to do with whether or how acupuncture works, nobody knows. In the West, acupuncture is primarily used for pain, but in China they use it for just about every illness. The research on it is demonstrating that it may be very useful for a variety of symptoms in addition to pain. The studies are small, and it's been very hard to have adequately blinded trials. It is possible to blind the patient to some degree, but it's been difficult so far to blind the persons delivering the acupuncture treatment.

In the studies so far, the most promising evidence is for acupuncture's role in treating nausea. There is enough evidence that many who have reviewed the studies would say that acupuncture is useful for nausea, especially postoperative nausea. *The Oslo Review on Research in Alternative Medicine* published an endorsement for acupuncture's effectiveness in nausea, chronic pain and post-stroke recovery but found no good evidence for its effectiveness in treating asthma or addiction treatment. The NIH Advisory Counsel on Alternative Medicine, in October 1997, recommends acupuncture treatment as effective for nausea and post-operative dental pain. The *American Journal of Chinese Medicine*[23] had a very good review this year that indicated that well-designed studies really need to be done because so many of the studies published have been poorly done. But there is clearly some positive evidence from some of the better trials that demonstrate that it is probably useful in tinnitus, angina, dry mouth, post-operative pain, migraine, dental pain, dysmenorrhea, tendinitis and low back pain and clear evidence of efficacy in nausea. Research into the mechanism of action of acupuncture is ongoing. Recently, a study using functional MRI imaging evaluated the eye acupuncture points, which are found in the foot. They showed brain activity in the visual cortex when the points in the foot that are used for eye illness are stimulated.

Acupuncture is generally very safe as long as practitioners use disposable needles. (When reusable needles were used, there was hepatitis and AIDS passed to patients.) Today, in developed countries complications are very rare.

Chiropractic

Chiropractic was started by a fellow named Daniel David Palmer in the late 1800s. He had apprenticed to be a M.D., which was a common method used to become a physician before they revised the medical education system and started to make students go to accredited schools. Mr. Palmer thought that there was a flow of Innate Intelligence through the body (which is a lot like ch'i, and the "vital force" of the other alternative disciplines). If there was interference with the flow, patients would fall sick, and cure could only ensue if the practitioner could eliminate the interference. This is accomplished by fixing "subluxations of the spine." This is the basic tenant of chiropractic.

To become a chiropractor, students must go through four years of chiropractic education after at least two years of college and then they are eligible to get a D.C. degree. Chiropractors are licensed in Hawaii. They also have specialization, with the addition of up to three years of additional training. Chiropractic students can specialize in internal medicine, radiology, sports medicine, orthopedics, neurology and nutrition.

There are different kinds of Chiropractors. There are two national organizations and they are called "Straights" and "Mixers" and there is a history of considerable conflict between the two types. Straights make up about 15% of chiropractors, and they are of the more old-fashioned school with the philosophy that **all** illness is caused by spinal subluxations. They consider themselves as primary care physicians, they treat all diseases and promote health with chiropractic manipulations. There are even colleges that include the designation "Straight Chiropractor" in their name to distinguish themselves from "mixers". The Mixers treat mostly back and musculo-skeletal pain, and sometimes may also use diet, herbs, homeopathy, and other treatments and are not purists who will only treat with spinal manipulation. The mixers are a much bigger group and they include the practitioners who just treat back problems with spinal manipulation, and refer everything else to other practitioners.

There is fellow from Hawaii named Kurt Butler who is a quack-exposer. He wrote a book about the dangers of alternative medicine, and he relates the following anecdote: In 1989, he went to twelve chiropractors who advertised free initial evaluations in the Honolulu newspaper. When he saw them, he indicated to each of them that he had symptoms of pressure-like chest pain when he walked with associated shortness of breath, and that he had epigastric abdominal pain at night that woke him up, which was relieved when he ate something and came on when he was hungry. So, he presented to them with symptoms of peptic ulcer disease and coronary artery disease, and yet none of them referred him to a doctor. All of them indicated a plan to treat him with chiropractic manipulation alone.[24]

Studies on the efficacy of spinal manipulation are conflicting, and most of them are of poor methodological quality. But there have been enough studies that have had positive results that the Agency on Health Care Policy and Research in the U.S. has recommended manipulation for acute low back pain, and the British version of our agency did the same.

Koes, et al., in *Spine* 1996, did a systematic review of randomized controlled trials of spinal manipulation for low back pain.[25] They pointed out in this review that this is one of many, and there are probably more reviews than there are actual studies about spinal manipulation for low back pain. They viewed 36 randomized controlled trials and compared spinal manipulation with other treatment. They used a complex methodological scoring system, with 100 being the best and 0 being the poorest. The study with the highest methodological score of all (which happened to be a study by Koes himself) was rated only 60 out of a 100. So, the quality in general is very poor. Of these studies, 53% or 19 of those studies showed favorable results for spinal manipulation. Of the 5 studies that had the top methodological scores (between 50 and 60), 3 were positive and 2 were positive in the subgroup only. There was no clear relationship between the methodology score, and whether the results were positive or negative. For acute low back pain, 5 were positive, 4 were negative and 3 were positive in the subgroup only. For subacute or chronic low back pain, 5 were positive, 2 were negative and 1 was questionable. So there is a tendency for manipulation to appear efficacious. In long term follow-up studies, 6 of 16 had a positive effect after 3 months. The conclusion was that we desperately need better trials.

There have been concerns about the safety of spinal manipulation, especially after a few case reports in the orthopedic journals of spinal transection from manipulation.[26, 27] However, the data available show a relatively good safety record for low back manipulation. There have been some cases of severe adverse effects from cervical manipulation that caused serious concern. However, the rate of adverse effect is low: most sources estimate 5 to 10 adverse events out of every 10 million spinal manipulations. The concern is that if adverse effects do occur, it could be to induce paraplegia, an obviously disastrous effect. One review of cervical manipulation's safety efficacy vs. NSAID-use safety and efficacy concluded that NSAID's efficacy for cervical neck pain has never actually been studied, so there is no efficacy data at all. Cervical manipulation, however, has been studied, and there is some evidence that it is efficacious. When risks were compared, even for serious life-threatening complications, NSAID use is statistically much riskier, probably a 100 times riskier than using cervical manipulation.[26]

Advice about Advising Patients

When advising patients about the use of alternative medicine, there are some opinions that can be given without concern about being inaccurate: one is that conventional medicine's ability to diagnose is clearly superior to any known alternative methods and should be utilized whenever the diagnosis is in question. Second, complementary treatments may have a very useful role when allopathic treatment is insufficient to relieve patients suffering, and when the patient won't accept any conventional treatment that has been recommended. Eisenberg, et al. in *Annals of Internal Medicine*,[28] published an article on how to advise patients on alternative medicine. He states that practitioners should ask non-threatening questions about "other" treatments used to treat illness or to maintain health, and to avoid the words "alternative" or "complementary," or other more pejorative terms (e.g., "unproven"). Only after a complete conventional medical diagnostic evaluation has been done and advice has been given about conventional treatment options, should a detailed discussion about alternative medical treatments be initiated.

Dr. Eisenberg considers the following therapies likely to be **effective**: spinal manipulation for low back pain, acupuncture for nausea, and relaxation therapy for chronic pain and insomnia. He

considered **risky**: spinal manipulation of the cervical spine, some herbs, "patent" remedies from uncontrolled places, restrictive diets, megadose vitamins, IM or IV substances and reusable needles. He considered **very low risk**: homeopathy, most massage, prayer, guided imagery, hypnosis, some herbs, and acupuncture with disposable needles. He advised to watch for indirect toxicity in the form of delay. There is also concern that some of these therapies, particularly prayer and guided imagery, can engender guilt and severe emotional duress because if the therapy fails, the patients can succumb to the idea that they were not "good enough" to get a benefit. Also, practitioners need to alert patients that drug-herb or drug-diet interaction can occur, for example, people on grapefruit diets can induce potentiation of calcium channel blockers, and in particular chemotherapy regimens may be rendered more toxic, or ineffective, due to concurrent use of alternative medicines. It is much preferable if patients are willing to try one thing at a time, so that efficacy can be assessed and to avoid increasing toxicity.

Eisenberg also outlines a step-by-step approach to helping patients try out alternative therapies with their physician's assistance to determine if the treatment has been effective and safe, and he recommend that physicians involve themselves in supporting patients' trials of treatments from a compassionate and evidence-based perspective. He recommends against referral based solely on patient demand, but only when it is part of a rational therapeutic plan. He advises that there are times when we must "agree to disagree," and he ends with the following statement: "No patient should feel that their medical journey is to be taken alone or according to some stealth trajectory, invisible to their conventional providers. The delivery of medical care, like the experience of illness is best viewed as a journey shared".[28]

CAM is a fascinating area of investigation and the practicing physician will need to keep abreast of the literature as studies are published. There is increasing funding support for research in this area, and conventional medical journals are likely to be publishing research about "alternative" practices in the coming years. As our knowledge base grows, it is likely to further blur the line between allopathic and complementary/alternative medicine; making the moniker "Integrative Medicine" a reality.

Acknowledgement

Appreciation is expressed to Linell Goya for secretarial and editorial services.

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